Chest radiography is a poor predictor of respiratory symptoms and functional impairment in survivors of severe COVID-19 pneumonia

Supplementary material

Methods

Table S1 Assessment of clinical, radiological, patient-reported and physiological COVID-19 sequelae

	Tool	Highest score	Cut off score	Time to complete
Clinical outcomes				
COVID-19 complications, healthcare utilisation	Electronic medical records, patient interview, physical examination	-	-	15 minutes
Radiological outcomes				
Chest radiograph resolution	Radiographic Assessment of Lung Oedema (RALE) score	48	Lung infiltrates absent/minimal defined as 0-4	1 minute
Thoracic computed tomography	Multidisciplinary team discussion	-	-	
Patient-reported outcomes				
Breathlessness, cough, fatigue, pain, sleep	Numerical Rating Scale	10	≥1 present ≥4 burdensome	<1 minute each
Breathlessness-related functional disability	Modified MRC Dyspnoea Scale	5	>1	1 minute
Disease-specific functional impairment	Post-COVID Functional Scale	4	≥2	1 minute
Depression	PHQ-9	27	>9	<3 minutes
Anxiety	GAD-7	21	>9	2-5 minutes
Post-Traumatic Stress Disorder	Trauma Screening Questionnaire	10	≥6	3 minutes
Cognitive impairment	6-Item Cognitive Impairment Test	28	≥8	5 minutes
Physiological outcomes				
Resting vital observations	Temperature, heart rate, oxygen saturation, blood pressure	-	-	2 minutes
Functional exercise performance	4-metre gait speed 1-minute sit-to-stand	-	<0.8m/s <2.5 percentile Desaturation ≥4%	3-5 minutes each

Persistent breathlessness, cough, fatigue, pain and sleep disturbance were measured using the 11-point Numerical Rating Score (NRS) [1-4]. For each symptom, patients selected an integer between zero (not present) and 10 (unbearable) that best reflected the intensity of the symptom in the preceding 24 hours. Symptoms were categorised as being present (score of ≥1) and burdensome (score of ≥4). Current and pre-COVID functional impairment was quantified using the 5-point modified Medical Research Council (mMRC) Dyspnoea Scale [5]. The 16-point Nijmegen Questionnaire was used to screen for hyperventilation syndrome and dysfunctional breathing (cut off score of 23) [6]. Anxiety and

depression screening was performed using the PHQ-9 and GAD-7 questionnaires, in which patients score 7 and 9 questions respectively between zero (not at all) to three ("nearly every day") using a cut-off score of >9 [7, 8]. The Trauma Screening Questionnaire was used to screen for post-traumatic stress disorder (PTSD), with patients asked to review 10 items and endorse those experienced at least twice in the preceding two weeks, using a cut off score of ≥6 [9]. The 6-Item Cognitive Impairment Test (6CIT) was used to screen for cognitive impairment [10]. The recently designed Post-COVID Functional Scale (PCFS) is a five-point scale used to reflect functional limitations during COVID-19 recovery and intended for use at 4-8 weeks and 6 months post-discharge [11].

Functional disability was objectively assessed using the 4-metre gait speed (4MGS) and 1-minute sit-to-stand (STS) test. Patients wore surgical masks continuously whilst on hospital premises, including during 4MGS and STS testing, thereby minimising aerosolisation of respiratory droplets. For the 4MGS, patients were timed whilst walking along an unobstructed 4-metre path at their usual speed, with their usual walking aids or oxygen if applicable, recording the fastest of two efforts and stratifying speeds as normal (≥0.8m/s) or slow (<0.8m/s). The 4MGS is a reliable and validated method of assessing exercise performance and frailty, and correlates with other tests of functional capacity, such as the incremental shuttle walk test, breathlessness and health-related quality of life (HRQoL) [12, 13]. For the STS, following a demonstration by the healthcare professional, patients were instructed to perform self-paced repetitions of sitting and standing from a chair for 1-minute. The number of repetitions, oxygen saturation and heart rate were recorded at baseline, end-exercise and during recovery, with repetitions categorised according to their percentile for age and sex [14]. The STS is a simple and highly reproducible measurement that correlates closely with other tests of functional capacity, including the 6-minute walk test (6MWT), and is predictive of mortality and HRQoL [15, 16]. Lung function testing was limited to urgent cases due to decontamination procedures required following this aerosol generating procedure [17].

Admission, worst inpatient and follow-up radiographs were graded using the Radiographic Assessment of Lung Oedema (RALE) score [18]. This involves review of consolidation and density of alveolar opacities in lung quadrants and produces a score between zero and 48. The RALE validation study was used to define radiological recovery as scores between 0 and 4 [18]. Patients with persistent radiological abnormalities, respiratory symptoms or desaturation of ≥4% during the STS underwent thoracic computed tomography (CT).

Results

Table S2 Baseline characteristics of all patients hospitalised with severe COVID-19 pneumonia between 5th March and 28th May 2020, those surviving to discharge and those attending Post-COVID assessment. Analyses represent comparisons between patients surviving to discharge and those attending Post-COVID assessment.

	All admissions (n=898)	Survived to discharge (n=657)	Post-COVID assessment (n=119)	Mean difference/ χ^2 (95% CI)	p-value
Age (years)					
Median (IQR)/ Mean± SD	68 (55-81)	64 (52-80)	58.7 ± 14.4	-6.1 (-9.2 to -3.0)	<0.001
18-29	34 (3.8; 2.6-5.0)	33 (5.0; 3.5-6.7)	4 (3.4; 0.8-6.7)		
30-39	42 (4.7; 3.5-5.9)	41 (6.2; 4.5-8.0)	11 (9.2; 5.0-14.3)		
40-49	70 (7.8; 6.2-9.4)	60 (9.1; 7.1-11.2)	13 (10.9; 6.7-15.1)		
50-59	159 (17.7; 15.1-20.4)	132 (20.1; 16.9-23.3)	36 (30.3; 22.7-38.7)	28.6 (0.17-0.29)	<0.001
60-69	168 (18.7; 16.4-21.3)	124 (18.9; 16.2-21.8)	27 (22.7; 16.0-28.6)		
70-79	160 (17.8; 15.6-19.9)	100 (15.2; 12.2-18.0)	18 (15.1; 10.1-21.0)		
80+	265 (29.5; 26.5-32.6)	167 (25.4; 22.1-28.7)	10 (8.4; 5.0-12.6)		
Sex (%)					
Female	385 (42.9; 39.2-46.3)	302 (46.0; 41.9-50.0)	45 (37.8; 29.4-46.2)	3.89 (0.01 to 0.15)	0.049
Male	513 (57.1; 54.1-60.4)	355 (54.0; 50.4-57.7)	74 (62.2; 53.8-70.6)		
Ethnicity (%)†					
BAME (Yes/No)	459/825 (55.6; 52.6-58.8)	329/600 (54.8; 50.8-59.1)	83/119 (69.7; 61.3-78.2)	36.2 (0.17 to 0.32)	<0.001
White	319 (35.5; 32.4-38.5)	224 (34.1; 30.4-37.8)	36 (30.3; 22.6-37.8)		
Black	378 (42.1; 39.1-45.3)	284 (43.2; 39.6-47.3)	52 (43.7; 36.1-51.3)		
Asian	51 (5.7; 4.2-7.0)	34 (5.2; 3.7-6.7)	18 (15.1; 10.1-20.2)	45.6 (0.20 to 0.36)	<0.001
Mixed race	17 (1.9; 1.2-2.6)	12 (1.8; 0.9-2.8)	5 (4.2; 1.7-6.7)		
Other	60 (6.7; 5.2-8.1)	46 (7.0; 5.1-9.0)	8 (6.7; 3.4-10.9)		
Not specified	73 (8.1; 6.5-9.9)	57 (8.7; 6.6-10.6)	0 (0)		
Median (IQR) / Mean±SD Index of multiple deprivation score ‡	29 (20-34) (n=893)	28.5 (20-34) (n=652)	26.6 ± 9.7 (n=115)	-1.0 (-3.0 to 0.92)	0.30
Body Mass Index (kg/m^2)					
Median (IQR)	27.0 (22.7-32.0)	27.7 (23.5-32.8)	30.0 (25.9-35.2)	2.7 (1.0 to 4.3)	0.005
Underweight (<18.5)	42/565 (7.4; 5.7-9.6)	30/482 (6.8; 4.7-9.1)	0/118 (0.0)		
Normal (18.5-24.9)	171/565 (30.3; 27.1-33.3)	125/482 (25.9; 22.3-29.8)	22/118 (18.6; 12.7-24.6)		
Overweight (25-29.9)	165/565 (29.2; 25.4-33.1)	150/482 (31.1; 26.8-35.2)	35/118 (29.7; 22.9-37.3)		
Obese (30-34.9)	104/565 (18.4; 15.6-21.6)	93/482 (19.3; 15.9-22.5)	30/118 (25.4; 19.5-33.1)	24.9 (0.18 to 0.32)	<0.001
Severely obese (35-39.9)	38/565 (6.7; 5.1-8.8)	45/482 (9.3; 6.9-12.0)	20/118 (16.9; 11.0-22.0)		
Morbidly obese (40-49.9)	36/565 (6.4; 4.8-8.1)	32/482 (6.6; 4.7-8.9)	9/118 (7.6; 4.2-11.0)		
Super obese (50+)	9/565 (1.6; 0.9-2.3)	7/482 (1.5; 0.4-2.6)	2/118 (1.7; 0.0-4.2)		
Comorbidities					
Median (IQR) Charlson comorbidity index‡	3 (1-5)	3 (1-5)	2 (1-4)	0.92 (0.44-1.36)	0.001
Any cardiovascular disease	431/659 (65.4; 61.8-68.7)	294/478 (61.5; 57.4-65.8)	57/119 (47.9; 40.3-55.5)	12.4 (0.07 to 0.25)	<0.001
Hypertension	405/651 (62.2; 58.8-65.6)	276/471 (58.6; 54.1-63.5)	54/119 (45.4; 37.8-53.8)	11.5 (0.06 to 0.25)	0.001
Ischaemic heart disease/ Heart failure	190/658 (28.9; 25.1-32.7)	120 /477 (25.2; 21.3-29.0)	8/119 (6.7; 3.4-10.1)	28.6 (0.17 to 0.31)	<0.001
Diabetes	264/655 (40.3; 36.6-44.1)	180/475 (37.9; 33.4-42.3)	41/119 (34.5; 26.4-42.9)	0.80 (0.00 to 0.13)	0.37
Chronic respiratory disease	246/654 (37.6; 33.7-41.3)	165/474 (34.8; 30.8-39.0)	13/119 (10.9; 6.7-16.0)	39.9 (0.22 to 0.36)	<0.001
Malignancy	80/654 (12.2; 9.9-14.5)	53/474 (11.2; 8.4-14.0)	12/119 (10.1; 5.9-14.3)	0.19 (0.00 to 0.10)	0.66
Cerebrovascular disease	153/654 (23.4; 20.5-26.3)	101/464 (21.3; 17.6-24.8)	5/119 (4.2; 1.7-6.7)	27.7 (0.18 to 0.30)	<0.001

Abbreviations: IQR = interquartile range, SD = standard deviation, BAME = Black, Asian, minority ethnic, χ^2 = Chi-square, 95% CI = 95% confidence interval

Table S3 Baseline characteristics and inpatient clinical course of post-COVID patients assessed between 3rd June and 2nd July 2020 compared to those who did not attend their scheduled assessment.

	Attended Post-COVID assessment (n=119)	Did not attend (n=24)	Mean difference/ χ^2 (95% CI)	p-value
Age (years)				
Mean ± SD	58.7 ± 14.4	57.7 ± 18.4	1.02 (-5.90 to 7.95)	0.81
18-29	4 (3.4; 0.8-6.7)	2 (9.1; 0.0-25.0)		
30-39	11 (9.2; 5.0-14.3)	3 (13.6; 0.0-31.6)		
40-49	13 (10.9; 6.7-15.1)	1 (4.7; 0.0-16.7)		
50-59	36 (30.3; 22.7-38.7)	6 (27.3; 8.3-47.6)	2.90 (0.12 to 0.40)	0.82
60-69	27 (22.7; 16.0-28.6)	4 (18.2; 3.7-35.7)		
70-79	18 (15.1; 10.1-21.0)	4 (18.2; 4.0-35.7)		
80+	10 (8.4; 5.0-12.6)	2 (9.1; 0.0-23.5)		
Sex (%)				
Female	45 (37.8; 29.4-46.2)	8 (33.3; 15.4-52.9)	0.17 (-0.14 to 0.20)	0.68
Male	74 (62.2; 53.8-70.6)	16 (66.7; 47.1-84.6)		
Comorbidities				
Cardiovascular disease	63 (52.9; 44.5-61.8)	3 (13.0; 0.0-29.4)	1.08 (-0.10 to 0.29)	0.30
Diabetes	41 (34.5; 26.4-42.9)	6 (26.1; 8.7-45.4)	0.61 (-0.22 to 0.09)	0.44
Obstructive lung disease	13 (10.9; 6.7-16.0)	3 (13.0; 0.0-30.0)	0.09 (-0.13 to 0.21)	0.77
Solid cancer	9 (7.6; 3.3-12.6)	1 (4.3; 0.0-14.3)	0.30 (-0.14 to 0.13)	0.58
Cerebrovascular disease	5 (4.2; 1.7-6.7)	5 (21.7; 5.3-40.0)	9.06 (0.02 to 0.49)	0.003
End stage renal failure	8 (6.7; 3.4-10.1)	2 (8.7; 0.0-21.4)	0.12 (-0.12 to 0.23)	0.74
Immunosuppressed	16 (13.4; 8.4-18.5)	4 (17.4; 3.4-33.3)	0.25 (-0.13 to 0.22)	0.62

Table S4 Additional inpatient complications

	Number (%)
Cardiac	
Fast atrial fibrillation	3 (2.5)
Myocarditis	2 (1.7)
Acutely impaired left ventricular function	2 (1.7)
Respiratory	
Pneumothorax	2 (1.7)
Pneumomediastinum	1 (0.8)
Haematological	
Venous thromboembolism	27 (22.7)
Pulmonary embolism	23 (19.3)
Deep vein thrombosis	6 (5.0)
Endocrine	
Hyperglycaemia	2 (1.7)
Diabetic ketoacidosis	1 (0.8)
New type 1 diabetes	1 (0.8)
Acute hyperthyroidism	1 (0.8)
Neurological	
Delirium	18 (15.1)
Subarachnoid haemorrhage	1 (0.8)
Intraparenchymal haemorrhage	1 (0.8)
Other	
Acute kidney injury	41 (34.5)
Deranged liver function tests	17 (14.3)
Neutropenic sepsis	1 (0.8)
Angioedema	1 (0.8)
Psoas haematoma	1 (0.8)
Sickle crisis requiring exchange transfusion	1 (0.8)
Upper gastrointestinal bleed	1 (0.8)

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